Complete Summary

GUIDELINE TITLE

Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources.

BIBLIOGRAPHIC SOURCE(S)

American College of Radiology (ACR). Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. Reston (VA): American College of Radiology (ACR); 2005. 13 p. [56 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Radiology (ACR). Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. Reston (VA): American College of Radiology (ACR); 2000.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- September 18, 2008. Phosphocol P 32 (chromic phosphate P 32 suspension): Covidien and Mallinckrodt Inc. informed healthcare professionals of important new safety information in prescribing Phosphocol P 32. Post marketing experience identified radiation injury (necrosis and fibrosis) to the small bowel, cecum, and bladder following administration of P 32 into the peritoneal cavity. Healthcare professionals should refer to the product's revised prescribing information for updated information regarding the appropriate use of Phosphocol P 32.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Medical conditions requiring therapy with radiopharmaceuticals:

- Hyperthyroidism (diffuse toxic goiter [Graves' disease], toxic nodular goiter, and solitary toxic nodule)
- Residual or metastatic thyroid cancer
- Myeloproliferative disorders such as polycythemia vera and thrombocytosis
- Malignant ascites
- Malignant pleural effusion
- Malignant pericardial effusion
- Malignant brain cysts
- Skeletal metastases
- B-cell non-Hodgkin's lymphoma

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Nuclear Medicine
Radiation Oncology
Radiology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To assist practitioners in providing appropriate radiologic care for patients
- To guide appropriately trained and licensed physicians performing therapy with unsealed radiopharmaceutical sources

TARGET POPULATION

Patients undergoing therapy with unsealed radiopharmaceuticals

INTERVENTIONS AND PRACTICES CONSIDERED

1. Qualifications and responsibilities of personnel
2. Examination and treatment including
    - General procedures (clinical evaluation, obtaining informed consent, quality management, radiation protection)
    - Iodine-131 (sodium iodide)
    - Strontium-89 and Samarium-153 Lexidronam
    - Phosphorus-32 (sodium phosphate or colloidal chromic phosphate)
    - Yttrium-90 Ibritumomab Tiuxetan and Iodine-131 Tositumomab
3. Follow-up after treatment
4. Documentation

MAJOR OUTCOMES CONSIDERED

Side effects and complications of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Each practice guideline and technical standard, representing a policy statement by the American College of Radiology (ACR), has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council.

This Practice Guideline for the Performance of Therapy with Unsealed Radiopharmaceutical Sources was revised by the ACR and the American Society for Therapeutic Radiology and Oncology (ASTRO).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines are approved by the Commission on Quality and Safety as well as the American College of Radiology (ACR) Board of Chancellors, the ACR Council Steering Committee, and the ACR Council.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Application of this guideline should be in accordance with the American College of Radiology (ACR) Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals, as that guideline relates to the handling of radiopharmaceuticals, radiation safety, and radiation protection of patients, personnel, and the public. There must also be compliance with applicable laws and regulations.

Definition

Therapy with unsealed sources involves administration of radiopharmaceuticals for the treatment of medical conditions.

Goal

The goal of therapy with unsealed radiopharmaceutical sources is to provide either cure or effective palliation of disease while minimizing untoward side effects and complications.

Indications

Examples of therapy with unsealed radiopharmaceutical sources are:

1. Iodine-131 (sodium iodide) for hyperthyroidism.
2. Iodine-131 (sodium iodide) for therapy of iodine-avid thyroid cancer.
3. Phosphorus-32 (sodium phosphate) for treatment of myeloproliferative disorders such as polycythemia vera and thrombocytosis.
4. Phosphorus-32 (colloidal chromic phosphate) for intracavitary therapy of malignant ascites, malignant pleural effusion, malignant pericardial effusions, and malignant brain cysts.
5. Strontium-89 (strontium chloride) and samarium-153 lexidronam ethylene diaminetetrame thylenephosphonic acid (EDTMP) for adjuvant and palliative treatment of painful skeletal metastases when these metastases are radiotracer-avid on a diagnostic bone scan.
6. Yttrium-90 ibritumomab tiuxetan and iodine-131 tositumomab, murine monoclonal antibodies that target the CD20 antigen, for treatment of patients with CD20 positive follicular B-cell non-Hodgkin's lymphoma, with or without transformation, that is refractory to rituximab and has relapsed following chemotherapy.

Qualifications and Responsibilities of Personnel

The qualifications and responsibilities of physicians and other personnel performing these therapeutic procedures should be in accordance with the ACR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals and/or the ACR Practice Guideline for Radiation Oncology. In addition, training and experience must be in compliance with the applicable laws and regulations.

Specifications of the Examination and Treatment

A. General Procedures
    1. Clinical Evaluation -- The initial evaluation of the patient includes history, physical examination, review of pertinent diagnostic studies and reports, and communication with the referring physician and other physicians involved in the patient's care. For the radiopharmaceutical treatments that are potentially marrow-toxic, a complete blood count

with differential should be part of the initial evaluation and of each pretreatment examination.

2. Quality Management -- In order to employ radiopharmaceuticals as unsealed sources for therapy, a "quality management" program must be in place as required by the Nuclear Regulatory Commission (NRC) or agreement state regulations. Key elements of this program are: written directives; duplicative procedures for identifying patients; careful record keeping to ensure correct administered activity; minimization of the possibility of infiltration for agents which are administered intravenously; procedures for minimizing radiation exposure or radiopharmaceutical contamination of personnel, family members of patients, and the public (e.g., alerts regarding possible current or future pregnancy); procedures for containment of radioactivity; and an audit mechanism to ensure compliance with the program.
3. Informed Consent -- Informed consent must be obtained and documented.
4. Treatment -- The procedure and follow-up should be performed according to an established system of procedural steps that may be unique for each type of application.
5. Female patients should not be pregnant or breast-feeding at the time radiopharmaceutical therapy is orally, intravenously, or intraperitoneally administered. Pregnancy should be ruled out by a negative human chorionic gonadotropin (hCG) test obtained within 72 hours prior to administration of the radiopharmaceutical or by documented history of hysterectomy or by a postmenopausal state with absence of menstrual bleeding for 2 years, or by premenarche in a child age 10 or younger. Breast-feeding should be completely discontinued prior to the therapy and should not be resumed until it has been determined safe to resume by the physician performing the therapy. After therapeutic doses of iodine-131, the NRC recommends no further breast-feeding until the next pregnancy. Other national regulatory bodies may have similar recommendations. The treating physician should also bear in mind that the immediate post-lactating breast may still concentrate iodine-131 resulting in breast radiation dose.
6. Radiation Precautions -- Radiation precautions and patient release criteria may be regulated federally by the U.S. Nuclear Regulatory Commission in many states, or by the state (with regulations that are closely patterned on the federal regulations and may be more restrictive). The radiation safety officer or health physicist for the local facility can provide information on the applicable regulations. Details on the federal regulations can be obtained at the NRC web site, www.nrc.gov, or by telephone (301-415-7000).

Refer to the original guideline document for additional information on radiation precautions.

B. Iodine-131 (sodium iodide). Therapy for Hyperthyroidism

The basic disease entities treated are: diffuse toxic goiter (Graves' disease), toxic nodular goiter, and solitary toxic nodule.

1. Diffuse Toxic Goiter
    a. Patient -- A recent radioiodine thyroid uptake should be available (see the ACR Practice Guideline for the Performance of Thyroid Scintigraphy and Uptake Measurements). The size of the thyroid gland should be estimated, either by palpation or by some other means. Optimally, the patient's system should be free of iodide-containing medications, iodinated contrast agents, exogenous thyroid hormone, and antithyroid medications.
    b. Administered Activities -- Initial activity of 50 to 200 microcuries (1.85-7.4 MBq) per gram of thyroid (after adjusting for current 24-hour radioiodine uptake) is usually administered. Generally the likelihood of residual hyperthyroidism is greater for lower administered activity, and the likelihood of hypothyroidism is greater for higher administered activity. There are also data to support empiric dosing with a "fixed" dose of 6.4 millicuries (240 MBq) or 9.5 millicuries (350 MBq). The limitation of fixed dose administration is that there is little correlation between the millicuries administered to the patient and the dose in cGy delivered to the thyroid gland due to the wide range of radioiodine uptake of hyperthyroid patients. The measurement of radioiodine uptake before radioiodine therapy is necessary even when a fixed dose is planned, to prevent the inappropriate administration of radioactive iodine to a patient with lymphocytic (silent) thyroiditis. Each treating physician, often in consultation with the referring physician, should decide on an appropriate activity to be administered (see Specifications of the Examination and Treatment section, A.6. in the original guideline document for radiation precautions).
    c. Side Effects/Complications -- Side effects are rare. Occasional exacerbation of thyro-toxicity may occur, which usually responds to short-term beta blocker medication. Patients may occasionally experience neck pain, tenderness, and/or odynophagia from radiation thyroiditis. Complications are also rare. Hypothyroidism is often considered the expected and desired outcome of successful therapy of Graves' disease or toxic nodular goiter and can occur within 2 months or decades later. Hypothyroidism is treated with carefully monitored hormone replacement therapy.
    d. Prior Thioamide Therapy -- Thioamides (e.g., propylthiouracil and methimazole) inhibit organification of iodide. If radioiodine therapy is administered during the first 2 weeks after discontinuing thioamide, the thyroidal absorbed dose is apt to be diminished due to more rapid iodine turnover. The iodine-131 dosage may need to be increased in these circumstances.
    e. Subsequent Therapies -- In patients who have not adequately responded to prior iodine-131 therapy, subsequent treatments may be given. A higher activity per gram of gland may be considered. Dose considerations should balance the total activity against the relative risks of residual disease versus hypothyroidism. Repeat therapies are usually not indicated until at least 3 months after a radioiodine treatment to allow the full effect to occur.

2. Toxic Nodular Goiter and Solitary Toxic Nodule
    a. Patient - See Specifications of the Examination and Treatment section, B.1.a. above.
    b. Administered Activity -- These conditions tend to be more resistant to radioiodine therapy. Activity of up to 30 or more millicuries (1.1 GBq) for outpatient treatment may be administered provided that the radioiodine uptake is sufficient.
    c. Side Effects/Complications -- See Specifications of the Examination and Treatment section, B.1.c. If a solitary toxic nodule has fully suppressed the function of the remaining thyroid, the risk of resulting hypothyroidism is decreased.
    d. Prior Thionamide Therapy -- The effect of thionamide on the responsiveness of the thyroid to radioiodine therapy is similar to that in diffuse toxic goiter. The treating physician should consider having the patient discontinue the medication to allow for systemic clearance or, if this is not feasible, using an activity in the upper end of the administered activity range.
    e. Treatment Failures -- Rarely, it may be necessary to administer an activity larger than 33.0 millicuries (1.2 GBq) in which case the patient may need to be confined and placed on radiation precautions (see Specifications of the Examination and Treatment section, A.6. in the original guideline document).

C. Iodine-131 (*S*odium Iodide). Therapy for Residual or Metastatic Thyroid Cancer

Iodine-avid thyroid cancers frequently take up radioiodine in the absence of significant amounts of residual normal thyroid tissue. In order to optimize ablative radioiodide therapy for residual or metastatic disease, or in selected cases to facilitate the follow-up for patients with good prognosis, the thyroid remnant should be completely eliminated by surgery and/or radioiodine treatment, if possible.

1. Ablation of Thyroid Remnant
    a. Patient -- The serum thyroid-stimulating hormone (TSH) must be elevated, usually to a level in excess of 30 microIU/mL, either by withholding oral thyroid hormone to induce endogenous TSH secretion or by injecting recombinant human TSH (rhTSH) to raise the patient's blood level of this hormone before therapy. If the remnant is suspected to be large, thyroid scintigraphy with technetium-99m (pertechnetate) or iodine-123 may be performed to determine how avidly the thyroid remnant is accumulating radioiodide. If the remnant is very small, a whole-body survey with iodine-131 or iodine-123 before ablation may be useful. Documentation of an elevated TSH level as well as adherence to a low iodine diet for 1 to 2 weeks prior to treatment are recommended. Optimally, the patient's system should be free of iodide-containing medications, iodinated contrast agents, exogenous thyroid hormone, and antithyroid medications. No age limits apply. Administration of more than 2 millicuries (74 MBq) of iodine-131 may interfere with subsequent uptake of iodine-131 for

several days to several weeks. This "stunning" effect may be minimized by administering the therapeutic dose within 72 hours of the activity administered for the diagnostic radionuclide dosage.

Refer to the original guideline document for information regarding Iodine-131 in known or suspected residual thyroid cancer, in distant metastases, and interactions with other forms of treatment. For information on side effects and complications of Iodine-131, refer to the Potential Harms field.

D. Strontium-89 and Samarium-153 Lexidronam. Therapy for Bone Pain Caused by Skeletal Metastases
    1. Patient -- Patients with multiple osseous metastases that show increased tracer uptake on bone scintigraphy, who are obtaining diminishing relief from other methods of pain management (e.g., analgesics, external beam irradiation), and whose bone marrow is competent, are candidates for radiopharmaceutical therapy. Patients with disseminated intravascular coagulation (DIC) must be excluded from therapy. Others may be treated after a case-by-case evaluation as adjuvant therapy to delay symptomatic skeletal metastases. Urinary incontinence is not a contraindication to treatment, although the patient or caregiver should be instructed on how to minimize radiation contamination from spilled urine. For samarium-153 lexidronam and strontium-89, bladder catheterization should be considered for patients incontinent of urine, to minimize the risk of radioactive contamination.
    2. Interactions with Other Forms of Treatment
        a. Hormone administration need not be discontinued before the administration of radiopharmaceutical therapy, since it does not interfere with the mechanism of action and does not potentiate any side effects.
        b. External beam radiation therapy may be used in concert with radiopharmaceutical therapy for local treatment of selected sites, especially those in which pathologic fracture or cord compression might occur.
        c. The patient should not have received long-acting myelosuppressive chemotherapy for 6 to 8 weeks and other forms of myelosuppressive chemotherapy for at least 4 weeks prior to radiopharmaceutical administration, also because of potential marrow toxicity.

    3. Retreatment -- Retreatment may be administered because of initial treatment failure or if symptoms recur. Special attention should be paid to recovery of bone marrow and blood counts. Retreatment may be given after adequate bone marrow recovery occurs, which is typically 2 to 3 months.
    4. As with all other forms of therapy with unsealed sources, patient management should be coordinated with clinical services and with other involved parties, especially radiation oncology, if external beam irradiation has been employed or is being considered.

Refer to the original guideline document for information on administered activities and radiation precautions and to the Potential Harms field for information on complications of Strontium-89 and Samarium-153.

E. Phosphorus-32 (Sodium Phosphate) for Polycythemia Rubra Vera or Thrombocytosis

Phosphorus-32 (sodium phosphate) is approved for treatment of polycythemia vera or thrombocytosis. The diagnosis must be confirmed prior to therapy. The activities may be standard (3.0 millicuries [111 MBq] intravenously) or based on body surface area (2.3 millicuries [85 MBq] per square meter intravenously) but should not usually exceed 5.0 millicuries (185 MBq). Relapse or failure to respond within 12 weeks may require retreatment with dosages up to 7.0 millicuries (259 MBq). Phosphorus-32 should not be given if the platelet count is less than 100,000/microliter or the leukocyte count is less than 3,000/microliter.

F. Phosphorus-32 (Colloidal Chromic Phosphate) for Malignant Ascites or Pleural Effusion

The usual activity for intracavitary therapy is 6 to 12 millicuries (222 to 444 MBq) in the pleural cavity and 10 to 20 millicuries (370 to 740 MBq) in the peritoneum. The ability of the radiopharmaceutical to spread uniformly throughout the affected cavity should be documented using technetium-99m sulfur colloid (see the ACR Practice Guideline for the Performance of Gastrointestinal Scintigraphy) as an intraperitoneal or intrapleural injection followed by appropriate imaging. The patient should be turned to distribute the imaging agent. After documented dispersal, the patient may be treated. The combination of intraperitoneal phosphorus-32 colloidal chromic phosphate and external irradiation to the pelvis has been reported to be associated with a high incidence of morbidity, particularly bowel obstruction; accordingly, caution must be observed when this combination of therapy is used.

G. Yttrium-90 Ibritumomab Tiuxetan and Iodine-131 Tositumomab for Radioimmunotherapy of Non-Hodgkin's Lymphoma
    1. Agents
        a. Yttrium-90 ibritumomab tiuxetan consists of ibritumomab, the murine immunoglobulin G1 (IgG1) kappa monoclonal antibody from which rituximab was developed, and tiuxetan, which stably chelates 111-In for imaging and 90-Y for therapy. Iodine-131 tositumomab is a murine IgG2a lambda monoclonal antibody covalently linked to iodine-131. Both antibodies are directed against the CD20 antigen which is found on the surface of normal and malignant B lymphocytes.

    2. Patient
        a. Patients with CD20 positive follicular B-cell non-Hodgkin's lymphoma, with or without transformation, including patients who are refractory to rituximab, are candidates for radioimmunotherapy.
        b. Patients must have two to three diagnostic scans prior to the therapeutic dose delivery in order to verify individual

biodistribution. In-111 ibritumomab tiuxetan is used for diagnostic studies prior to treatment with yttrium-90 ibritumomab tiuxetan, and a diagnostic activity of iodine-131 tositumomab is used prior to the therapeutic dose delivery of that radiopharmaceutical. Patients with altered biodistribution as described in paragraphs 3.b and 3.c of this section in the original guideline document should not be treated with these radiopharmaceuticals. The pretreatment scans are also used to calculate the therapeutic dose for iodine-131 tositumomab.

c. Patients treated with iodine-131 tositumomab are at risk for hypothyroidism. To reduce this probability, they must be treated with either a saturated solution of potassium iodide (SSKI) four drops orally a day, Lugol's solution 20 drops orally three times a day, or potassium iodide tablets 130 mg orally once a day, starting at least 24 hours prior to initiating the iodine-131 tositumomab dosimetric dose. Thyroid blockade must continue until 2 weeks after administration of the iodine-131 tositumomab therapeutic dose.

3. Dosimetry and assessment of biodistribution

   See the original guideline document for more information on this topic.

4. Administered activity

   See the original guideline document for more information on this topic.

5. Complications

   See the "Potential Harms" section of this summary for more information on this topic.

6. Interactions with Other Forms of Treatment
   d. A time interval sufficient to allow for bone marrow recovery after cytotoxic chemotherapy is recommended. Concomitant use of chemotherapy with yttrium-90 ibritumomab tiuxetan or iodine-131 tositumomab therapy has not been fully evaluated.
   e. Prior to radiopharmaceutical therapy, external beam radiation therapy may be necessary for local treatment of selected sites, especially when life-threatening or function-threatening involvement such as fracture or spinal cord compression exists or is likely to occur without such treatment. Careful consideration must be given to the amount of bone marrow treated, as treatment of a large percentage of the patient's bone marrow is likely to significantly affect the ability to tolerate radioimmunotherapy.

7. Radiation precautions

   See the original guideline document for more information on this topic.

8. As with all other forms of therapy with unsealed sources, patient management should be coordinated with clinical services and with other involved parties, especially medical and radiation oncology.

H. Follow-Up after Treatment

Physicians using unsealed radiopharmaceutical sources for therapy should follow up and manage all patients treated with curative, adjuvant, or palliative intent and document the outcome of therapy, including results of treatment (tumor control, survival, degree of palliation, time to retreatment) and significant sequelae. Patients who are treated with palliative intent may require close follow-up. For patients for whom follow-up is not possible, there should be documentation specifying which physician will be responsible for the patient's ongoing care.

Documentation

Reporting should be in accordance with the ACR Practice Guideline for Communication: Radiation Oncology.

ACR Statement on Therapeutic Use of Unsealed Radiopharmaceutical Sources

It is the position of the American College of Radiology that both nuclear medicine physicians and radiation oncologists are particularly well qualified by training and experience to administer unsealed radiopharmaceutical sources for treatment and that either can do so independently. Often, the preferred approach is for the nuclear medicine physician and radiation oncologist to work together as a physician team. The approach that is chosen may vary from patient to patient depending on the type of cancer being treated, local expertise, and patient-related issues. Whichever approach is used, it is important that patient selection as well as overall treatment planning and follow-up be performed by physicians with training and expertise in cancer management, basic radiation safety, and radiation physics.

Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns

See "Description of the Implementation Strategy" field, below.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- The goal of therapy with unsealed radiopharmaceutical sources is to provide either cure or effective palliation of disease while minimizing untoward side effects and complications.
- Adherence to this guideline should help to maximize the efficacious use of radiopharmaceutical therapy and management of the attendant side effects, maintain safe conditions, and ensure compliance with applicable regulations.

POTENTIAL HARMS

Side Effects and Complications of Radiopharmaceutical Therapy

Iodine-131 (Sodium Iodide) for Hyperthyroidism

- Side effects are rare. Occasional exacerbation of thyro-toxicity may occur, which usually responds to short-term beta blocker medication. Patients may occasionally experience neck pain, tenderness, and/or odynophagia from radiation thyroiditis. Complications are also rare.
- Thioamides (e.g., propylthiouracil and methimazole) inhibit organification of iodide. If radioiodine therapy is administered during the first 2 weeks after discontinuing thioamide, the thyroidal absorbed dose is apt to be diminished due to more rapid iodine turnover. The iodine-131 dosage may need to be increased in these circumstances.

Iodine-131 (Sodium Iodide) for Residual or Metastatic Thyroid Cancer

Hypothyroidism, which is usually present prior to iodine-131 therapy as a result of surgery, is an expected result. Side effects include radiation dysphagia and sialadenitis, both of which are activity related and self-limited. To prevent sialadenitis, measures should be taken to stimulate salvia flow for 1 to 2 days following therapy, such as recommending administration of a sialogogue or other agent that stimulates the salivary glands. With larger activities or multiple administrations, xerostomia may rarely occur. Patients given 100 millicuries (3.7 GBq) or more may develop mild treatment-related symptoms such as headache, nausea, and vomiting that begin about 4 hours after iodine-131 administration and resolve within 72 hours. Diarrhea has occasionally been noted. A single dose of 50 to 100 millicuries (1.85 to 3.7 GBq) may deliver sufficient radiation to the testes to cause transient testicular failure of uncertain long-term consequence. Sperm banking or discussion of fertility issues should be considered, particularly in young men for whom the cumulative dose is anticipated to be over 100 millicuries (3.7 GBq) or who may need multiple treatments. There is some evidence that female fertility may be decreased after activities in excess of 600 millicuries. Myelosuppression may occur with oral doses of iodine-131 in excess of 150 to 200 millicuries, and Dosimetry I suggested when such doses are used, especially in older patients. Leukemogenesis and carcinogenesis (salivary glands, kidney, bladder, gastrointestinal tract) have been described in patients following high dose iodine-131 therapy.

Strontium-89 and Samarium-153 Lexidronam

- Bladder catheterization should be considered for patients incontinent of urine, to minimize the risk of radioactive contamination.
- A "flare" phenomenon occurs in some patients, with transient worsening of pain within several days. It may last several days and can be severe, although the pain usually improves when compared to pretreatment level. It may be managed with analgesic or steroidal medication. Extravasation of the radiopharmaceutical should be avoided, and it is imperative to have excellent intravenous access that is functioning properly prior to injection. Bone marrow depression occurs transiently, with a nadir at about 3 to 6 weeks and with recovery in about 3 to 6 additional weeks. Complete blood and platelet counts should be followed routinely for 8 to 12 weeks.
- The patient should not have received long-acting myelosuppressive chemotherapy for 6 to 8 weeks and other forms of myelosuppressive chemotherapy for at least 4 weeks prior to radiopharmaceutical administration, because of potential marrow toxicity.

Phosphorus-32 (Colloidal Chromic Phosphate)

The combination of intraperitoneal phosphorus-32 colloidal chromic phosphate and external irradiation to the pelvis has been reported to be associated with a high incidence of morbidity, particularly bowel obstruction; accordingly, caution must be observed when this combination of therapy is used.

Yttrium-90 Ibritumomab Tiuxetan and Iodine-131 Tositumomab

- Hypersensitivity reactions occur and may be severe. Patients who have received murine proteins should be screened for human antimouse antibodies. Patients who are positive are likely to be at increased risk of anaphylaxis and serious hypersensitivity and may show altered biodistribution of the antibody. Premedication with acetaminophen and diphenhydramine is recommended and should be considered prior to both indium-111 ibritumomab tiuxetan and yttrium-90 ibritumomab tiuxetan. Medications for the treatment of hypersensitivity reactions (e.g., epinephrine, antihistamines, and corticosteroids) and equipment for resuscitation should be immediately available.
- The most common serious adverse reactions associated with both yttrium-90 ibritumomab tiuxetan and iodine-131 tositumomab are severe or life-threatening cytopenias. With yttrium-90 ibritumomab tiuxetan, approximately 85% of patients are expected to experience grade 3 or 4 cytopenia. With iodine-131 tositumomab, 71% of 230 patients enrolled in clinical studies experienced grade 3 or 4 cytopenias. The nadir can occur from 1 to more than 3 months after administration, and the duration of cytopenias can be from 3 to 5 weeks. Precautions include not treating patients who have more than 25% of bone marrow involved, or who have poor bone marrow reserve (including but not limited to prior stem-cell or bone marrow transplant, absolute neutrophil count <1,500 cells/microliter, or previous failure of stem cell collection). The dose is modified according to the pretreatment platelet counts. Blood counts are monitored weekly or more frequently as needed until recovery occurs, for at least 10 to 12 weeks. Stem cell support and/or

transfusions are provided as necessary, and cases of febrile neutropenia or infection are treated as appropriate.
- In patients treated with iodine-131 tositumomab, hypothyroidism occurs approximately 5% of the time despite thyroid protection.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Therapy with unsealed radiopharmaceuticals is contraindicated in pregnancy and breast-feeding.
- Patients with disseminated intravascular coagulation must be excluded from therapy with *Strontium-89 and Samarium-153 Lexidronam*
- Phosphorus-32 should not be given if the platelet count is less than 100,000/microliter or the leukocyte count is less than 3,000/microliter.
- Known hypersensitivity to rituximab or murine proteins is considered a contraindication to administration of yttrium-90 ibritumomab tiuxetan.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth in the guideline, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.
- The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care.
- To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.
- The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The

sole purpose of these guidelines is to assist practitioners in achieving this objective.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns

Policies and procedures related to quality control and improvement, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Medical Nuclear Physics Performance Monitoring of Nuclear Medicine Imaging Equipment.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American College of Radiology (ACR). Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. Reston (VA): American College of Radiology (ACR); 2005. 13 p. [56 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2005)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Radiology

GUIDELINE COMMITTEE

Collaborative Subcommittee
Guidelines and Standards Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Radiology (ACR). Practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. Reston (VA): American College of Radiology (ACR); 2000.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR practice guidelines and technical standards purpose and intended use. Reston (VA): American College of Radiology; 1 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- The process for developing ACR practice guidelines and technical standards. Reston (VA): American College of Radiology; 1 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 21, 2007. The information was verified by the guideline developer on May 29, 2007. This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Phosphocol P 32.

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